

CLAIMS

1. A method for delivery of a therapeutic neurotrophin to targeted defective, diseased or damaged cholinergic neurons in the mammalian brain, the method comprising delivering a neurotrophic composition, comprising a neurotrophin encoding transgene, into one or more delivery sites within a region of the brain containing targeted neurons; wherein the transgene is expressed in, or within 500  $\mu$ m from, a targeted cell, and no more than about 10 mm from another delivery site; and wherein further contact with the neurotrophin ameliorates the defect, disease or damage.

2. The method according to Claim 1, wherein the transgene is expressed by a viral expression vector.

3. The method according to Claim 2, wherein the viral expression vector is an adenovirus.

4. The method according to Claim 2, wherein the viral expression vector is an adeno-associated virus.

5. The method according to Claim 2, wherein the viral expression vector is a lentivirus.

6. The method according to Claim 2, wherein the viral expression vector is HIV-1.

7. The method according to Claim 2, wherein the neurotrophic composition is a fluid having a concentration of neurotrophin encoding viral particles in the range from  $10^{10}$  to  $10^{15}$  particles per ml of neurotrophic composition.

8. The method according to Claim 7, wherein from 2.5  $\mu$ l to 25  $\mu$ l of the neurotrophic composition is delivered to each delivery site.

9. The method according to Claim 8, wherein delivery to each delivery site is accomplished over a period of time greater than or equal to 3 minutes.

5 10. The method according to Claim 9, wherein delivery to each delivery site is accomplished over a period of time less than or equal to 10 minutes.

11. The method according to Claim 1 wherein the treated mammal is a human and the transgene encodes a human neurotrophin.

10 12. The method according to Claim 11 wherein the neurotrophin is human beta nerve growth factor ( $\beta$ -NGF).

13. The method according to Claim 11 wherein the neurotrophin is human neurotrophin 3 (NT-3).

15 14. The method according to Claim 1 wherein the delivery sites are intraparenchymal.

15. The method according to Claim 1 wherein the delivery sites are within the Ch4 region of the cholinergic basal forebrain.

16. The method according to Claim 1 wherein the transgene is expressed by a non-viral expression vector.

20 17. The method according to Claim 1 wherein the ameliorated disease is Alzheimer's disease.